

PTO/SB/21 (08-00)

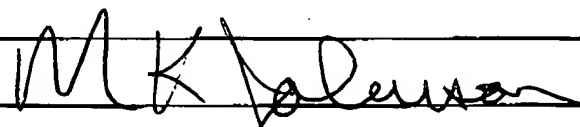
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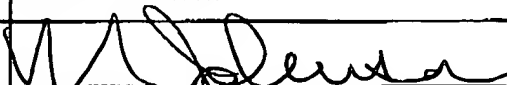
TRANSMITTAL FORM <i>(to be used for all correspondence after initial filing)</i>	Application Number	09/881,326	
	Filing Date	06/14/2001	
	First Named Inventor	David Rozema	
	Group Art Unit	1636	
	Examiner Name	William Sandals	
Total Number of Pages in This Submission	4	Attorney Docket Number	Mirus.013.04.02

ENCLOSURES (check all that apply)		
<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input checked="" type="checkbox"/> Amendment / Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Assignment Papers (for an Application) <input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s)	<input type="checkbox"/> After Allowance Communication to Group <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input type="checkbox"/> Other Enclosure(s) (please identify below)
<div style="text-align: right; font-weight: bold; font-size: 1.2em;">PAX RECEIVED</div> <div style="text-align: right; font-weight: bold; font-size: 1.2em;">JAN 21 2003</div> <div style="text-align: right; font-weight: bold; font-size: 1.2em;">OFFICIAL GROUP 1600</div>		
Remarks Attached is a signed copy of the originally faxed Supplement.		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Mirus Corporation
Signature	
Date	01/20/2003

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being sent by facsimile transmission to art unit 1636, 703.308.4242, and addressed to: Commissioner for Patents, Washington, DC 20231 on this date:		01/20/2003
Typed or printed name	Mark K. Johnson	
Signature		Date
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Jon A. Wolff,
James E. Hagstrom, Sean D. Monahan,
Paul M. Slattum, David B. Rozema and
Vladimir G. Budker

Serial No.: 09/881,326

,Filed: 06/14/2001

Group Art Unit: 1636

Examiner: William Sandals

For: Intravascular Delivery of Non-Viral Nucleic Acid

SUPPLEMENTAL INFORMATION

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Applicants have attached information that they believe is pertinent to the examination of this case. In particular, the information has been copied from the file history of the U.S. Patent No. 5,698,531 issued to Nabel *et al.* which is the primary prior art cited in Applicants' case.

Applicants wish to supplement their argument that the '531 patent does not teach transfection of extravascular parenchymal cells. The information provided also supplements the telephone interview held on Thursday, January 16, 2003 between Applicants and the Examiner where Applicants call attention to an article reviewing the state of gene delivery published by Elizabeth Nabel (Circulation. 1995;91:541-548.). Elizabeth Nabel states on page 544, 1st column, last paragraph:

"Several observations concerning the delivery of recombinant genes and patterns of gene expression can be drawn from these studies. Infusion of vector into normal arteries with an intact endothelium results in transfection of intimal cells (primarily endothelial cells). [at this point, Ms. Nabel cites her own work among others published well after the filing date of the '531 patent.] Injury to the vessel and/or application of pressure to the vector infusate results in delivery of DNA transmurally and gene expression in the media".

This paragraph dictates the overall extent of transfection into blood vessels in 1995 as well as the '531 inventors' ability to 'teach' the art in years prior to 1995: 1) transfection

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into intimal cells (1st layer of vasculature without injury; and 2) transfection into medial cells (2nd layer of vasculature) with injury.

As further evidence of the '531 inventors' lack of ability to teach Applicants' delivery methods, Applicants call the Examiner's attention to the file history of the '531 patent. In the amendment filed on November 22, 1993, page 3, the inventors limit their teachings to "site-specifically transforming cells." On page 5 site-specificity is limited to "using physical methods to place the DNA or RNA sequences at specific locations." On page 10 of the '531 amendment, the inventors provide data to show delivery to vessel cells and lack of delivery to extravascular cells by β -galactosidase activity: "In addition, no β -galactosidase activity was observed in random microscopic segments from the liver, lung, or kidney, except for cells with endogenous activity."


Importantly, on page 19 of the same amendment, the '531 inventors attempt to differentiate their process from a prior art process and thereby limit their '531 teachings to a physical method of delivery (injury to the endothelial wall): "Firstly, Myers [prior art to Nabel *et al.*] differs from the present invention in that it uses the vector as a homing beacon to ensure that the DNA sequence reaches the appropriate cell. In contrast, the present invention uses physical methods to deliver recombinant genes to specific lesions *in vivo* and differs from Myers targetable injectable vector." Applicants point out that in the '531 inventors' own language they state that they must deliver to "specific lesions" which are caused by their denuding processes and differs from an injectable vector.

In a further limitation to the '531 teachings, Paper 19, an Office Action to the '531 inventors, states on page 2: "Clearly a syringe, as would be used for injection purposes, would be materially distinct from the balloon catheter". In Paper 26, an examiner interview summary record attempts to convince Nabel *et al.* to "reduce issues of prior art" by limiting their claims to a balloon catheter, stating: "Examiner suggested bringing out balloon catheter concept in the method claims." Nabel *et al.* respond and finally limit their claims to a catheter.

By their own statements, the inventors of the '531 patent have limited their teachings to physical denuding of vessel walls followed by physical delivery to specific locations of a vessel wall. One would have to ignore logic to conclude that the '531 patent teaches non-local delivery of genetic material to extravascular parenchymal cells by injection as taught by Applicants.

Applicants request that the Examiner contact them regarding this correspondence after his consideration.

Respectfully submitted,


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I hereby certify that this correspondence is being sent
by facsimile transmission to art unit 1636,
703.308.4242: Commissioner for Patents,
Washington, DC on Thursday, January 16, 2003.


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